EXHIBIT HH

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1390 Piccard Drive
Rockville, MD 20850

OCT 12 1990

Mr. James P. O'Donnell
Manager
Regulatory Affairs
Ethicon, Inc.
P.O. Box 151
Somerville, New Jersey 08876-0151

REGULATORY AFFAIRS
OCT 15 1990
RECEIVED

Re: N16374
PROLENE™, Polypropylene Nonabsorbable Suture

Dear Mr. O'Donnell:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) reclassified the nonabsorbable poypropylene surgical suture on July 5, 1990, effective on that date, from Class III into Class II (order enclosed). Notice of this reclassification will be announced in a future Federal Register notice. This letter constitutes notification that devices approved for commercial distribution under your PMA, N16374 and supplements 1 through 35, of your PMA, have also been reclassified into Class II.

FDA identified nonabsorbable polypropylene surgical suture as follows:

> Nonabsorbable polypropylene surgical suture is a monofilament, nonabsorbable, sterile, flexible thread prepared from long-chain polyolefin polymer known as polypropylene and is intended for use in soft tissue approximation. The polypropylene surgical suture meets USP requirments as described in the USP Monograph for Nonabsorbable Surgical Sutures; it may be undyed or dyed with an FDA approved color additive; and the suture may be provided with or without a standard needle attached.

Accordingly, FDA has determined that your devices, as approved for marketing under your PMA and PMA supplements, are included in this generic type of device and are, therefore, reclassified into Class II. Although your devices were originally approved under an NDA/PMA application for commercial distribution, you may continue to market your devices subject to the general controls provisions of the Federal Food, Drug, and Cosmetic Act (act) and any performance standards promulgated under section 514 of the act. As such, any new device or any modification to your existing device(s) is subject to the premarket notification provisions of 21 CFR 807.81, and may require a determination of substantial equivalence in order to be marketed.

If you have any questions, please contact Kenneth A. Palmer, Ph.D., at (301) 427-1090.

Sincerely yours,

Robert L. Sheridan
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1390 Piccard Drive
Rockville, MD 20850

JUL 5 1990

Mr. Walter S. Hennig
Vice President, Quality Functions
United States Surgical Corporation
150 Glover Avenue
Norwalk, Connecticut 06856

Re: Reclassification of Nonabsorbable Polypropylene Surgical Suture, Docket Number 88P-0173

Dear Mr. Hennig:

INTRODUCTION

The Center for Devices and Radiological Health (CDRH) for the Food and Drug Administration (FDA) has completed its review of your reclassification petition for the nonabsorbable polypropylene surgical suture. FDA concludes that the generic type of device, nonabsorbable polypropylene surgical suture, and all devices substantially equivalent to this generic type, should be reclassified from class III into class II with a low priority for the development of a performance standard. This order, therefore, reclassifies nonabsorbable polypropylene surgical sutures into class II effective immediately.

FDA identifies the generic type of device the subject of this reclassification, as follows:

> Nonabsorbable polypropylene surgical suture is a monofilament, nonabsorbable, sterile, flexible thread prepared from long-chain polyolefin polymer known as polypropylene and is indicated for use in soft tissue approximation. The polypropylene surgical suture meets USP requirements as described in the USP Monograph for Nonabsorbable Surgical Sutures; it may be undyed or dyed with an FDA approved color additive; and the suture may be provided with or without a standard needle attached.

As you know, on May 4, 1988, FDA filed the reclassification petition submitted by Advanced Biosearch Associates of Danville, California on your behalf requesting reclassification of nonabsorbable polypropylene surgical suture from class III into class II. The petition was submitted under section

520(1) of the Federal Food, Drug and Cosmetic Act ("act"), 21 U.S.C. 360j(1), seeking reclassification under the procedures set forth in section 520(1)(2) of the act, 21 U.S.C. 360j(1)(2), and 21 CFR 860.136 of the agency's regulations.

Consistent with the act and the regulations, the agency consulted with the General and Plastic Surgery Devices Panel ("Panel") regarding the reclassification petition. The agency, by its September 28, 1988 letter and statements at the panel meeting, fully briefed the Panel about its obligations regarding the reclassification petition for nonabsorbable polypropylene surgical suture that was before it. The Panel, during an open public meeting on October 20, 1988, recommended that FDA reclassify nonabsorbable polypropylene surgical suture from class III into class II, and that FDA assign a high priority to the development of a performance standard for the generic type of device under section 514 of the act, although a performance standard need not be in place before reclassification is effective (Ref. 8 at page 55).

After reviewing all data in the petition and presented before the Panel, and after fully considering the Panel's recommendation and the views of the participants at the panel meeting, FDA, based on the information set forth in this letter, is ordering the reclassification of the generic type of device, identified on page 1, supra, from class III to class II.

RECLASSIFICATION PROCEDURE

Reclassification of nonabsorbable polypropylene surgical suture is governed by section 520(1) of the act, 21 U.S.C. 306j(1). The nonabsorbable polypropylene surgical suture is regulated as a class III device because prior to the Amendments it was subject to an approved "new drug" application submitted under section 505(b). See Section 520(1)(1)(A). Devices subject to "new drug" approvals prior to the Amendments are known as transitional devices and are automatically placed into class III to assure continuity of regulation.

Section 520(1)(1)(D), likewise, automatically classifies into class III a device that is "within a type of device described in subparagraph (A), (B), or (C) [of section 520(1)(1)] and is substantially equivalent to another device within that type." No time or other limitations narrow the scope of section 520(1)(1), nor is it suggested by the statute's text that anything other than all devices that fit within the scope of section 520(1)(1) are to be considered transitional, class III devices. Therefore, nonabsorbable polypropylene surgical sutures that are introduced well after the enactment date of the Amendments, which are substantially equivalent to a suture classified under section 520(1)(1)(A), are classified into class III under the authority of section 520(1)(1)(D).

Section 520(1)(2) of the act, which sets forth the procedures for reclassification of devices classified under section 520(1)(1), unambiguously applies to all devices classified under that section, and its scope is no more limited than that of section 520(1)(1). The statute's language is clear that section 520(1)(2) of the act is the exclusive means for reclassifying a device

classified under section 520(l)(1). Nothing in the act suggests that transitional device reclassification should be initiated under any section of the act other than section 520(l)(2).

The act's premarket notification requirement demonstrates further that this proceeding is authorized by the transitional device reclassification provisions. If any person were to file a premarket notification under section 510(k) of the act, 21 U.S.C. 360(k), he would be required to identify:

> The class in which the device is classified under section 513 or if such person determines that the device is not classified under such section, a statement of that determination and the basis for such person's determination that the device is or is not so classified (emphasis added). Id.

Clearly, nonabsorbable polypropylene surgical suture was not classified under section 513. Congress, as evidenced by the underlined portion of the above-quoted language, recognized that classification could occur outside of section 513. Section 520(l)(1) provides the only means of classifying a device outside of section 513 available under the act, and nonabsorbable polypropylene surgical suture was classified under the authority of that section. Accordingly, any person now bringing nonabsorbable polypropylene surgical suture to the market for the first time would be required to inform the agency in the context of section 510(k) of whether his nonabsorbable polypropylene surgical suture is substantially equivalent to a preamendment suture, as classified under section 520(l)(1), or a unique and, therefore, "new" suture as classified under section 513(f)(1).

For the nonabsorbable polypropylene surgical suture the subject of this reclassification proceeding, it is unchallenged that it was classified into class III under section 520(l)(1). Accordingly, since neither sections 520(l)(1) nor 520(l)(2) express any time restraints or other limitations regarding the acts of classification or reclassification of transitional devices, and since the Amendments, through premarket notification, intend that substantially equivalent devices, including transitional devices, be classified the same, I must conclude that the agency's position, that section 520(l)(2) describes the reclassification procedures for devices originally classified under section 520(l)(1), is reasonable and should be followed.[1]

---

[1] The agency's understanding of the transitional device provision is consistent with the act and the agency's regulations, and is also supported by legislative history, stating:

> [the] [o]pportunity to petition [under the transitional device provisions] for reclassification to class II or I is afforded the manufacturer or importer of any device classified into class III as a result of [section 520(l)(1).]

H.R. Rep. No. 853, 94th Cong., 2d Sess., February 29, 1976 at 38.

As the above discussion demonstrates, Congress intended to permit persons, who for the first time desire to manufacture or import transitional devices, the opportunity to seek reclassification under section 520(l)(2), notwithstanding the fact that reclassification was sought well after the passage of the Amendments. Moreover, U.S. Surgical, in our view and as the record shows, is an appropriate party to petition for reclassification under section 520(l)(2) in that the company intends to market nonabsorbable polypropylene surgical suture, and presently has received approval from FDA to export nonabsorbable polypropylene surgical suture to Italy, West Germany, France, The Netherlands and Switzerland (Ref. 150). Under these circumstances, U.S. Surgical, like any person submitting a premarket notification under section 510(k) seeking classification under section 520(l)(1), has standing to pursue reclassification under section 520(l)(2) from an automatic class III placement.

DECISION

After reviewing the publicly available literature in the record, the Panel's deliberation, and FDA's past actions regarding nonabsorbable polypropylene surgical suture, it is apparent to FDA that a class III designation for nonabsorbable polypropylene surgical suture constitutes overregulation.

By limiting the generic class, the subject of this order, to nonabsorbable polypropylene surgical suture, as defined on page 1, FDA, according to the record evidence, has limited this reclassification to nonabsorbable polypropylene surgical suture with the same or similar health risks. This approach is entirely consistent with FDA's definition of a generic type of device, see 21 CFR 860.3(i), and its view that "[t]he similarity of health risks is fundamental to the concept of classification by generic type of device," see 43 Fed. Reg. 32989, 32992 (July 28, 1978).

Additionally, U.S. Surgical has provided information in its petition to show that, despite variations in nonabsorbable polypropylene surgical suture materials and manufacturing processes, test methods exist to demonstrate whether any nonabsorbable polypropylene surgical suture is within the scope of the generic type of device identified in this order. Therefore, we believe that the nonabsorbable polypropylene surgical suture is well characterized and an appropriate candidate for reclassification.

As you have demonstrated, class II controls are appropriate to regulate nonabsorbable polypropylene surgical suture. Class II controls are indicated where class I controls alone are inadequate to reasonably assure a device's safety and effectiveness, and sufficient information exists to establish a performance standard to provide for such an assurance. See section 513(a)(1)(B) of the act, 21 U.S.C. 360c(a)(1)(B). As our discussion below demonstrates, the publicly available valid scientific evidence contained in the administrative record in this matter identifies the performance parameters and risks that define the safety and effectiveness of nonabsorbable polypropylene surgical suture. Also, valid scientific evidence in the record demonstrates the basis of a performance standard to control these parameters and risks and, thus, "sufficient information to establish a performance

standard," (see section 513(a)(1)(B)), exists to classify nonabsorbable polypropylene surgical suture into class II.

A class II classification may occur with or without an actual standard being in place. Of importance is the fact that enough is known about the performance of nonabsorbable polypropylene surgical suture that the generic premarket clearance criteria of a performance standard constitute a more appropriate level of regulatory control than the agency's product by product premarket review, mandated by class III controls. Indeed, the data in the record show that when weighing benefits to the probable risk of illness or injury resulting from the use of nonabsorbable polypropylene surgical suture, class III controls are unnecessary to assure the device's safe and effective performance.

In granting your petition, FDA has relied on valid scientific evidence, as defined by 21 CFR 860.7(c)(2). The agency's regulations prescribe various types of evidence that may be valid scientific evidence, including, for example, well-controlled studies and reports of significant human experience with marketed devices. Although a well-controlled investigation is a component of valid scientific evidence, it is important to appreciate that such an investigation is but one type of evidence that can be relied upon by FDA to make classification and other regulatory decisions.

FDA firmly believes that end-product test methods are available to thoroughly evaluate nonabsorbable polypropylene surgical suture, and that publicly available valid scientific evidence supports this conclusion. The agency contrues section 514 of the act to sanction the use of end-product testing as a means of evaluating the properties and performance of a device. In that nonabsorbable polypropylene surgical suture is considered by the agency to be well characterized, and the record evidence supports this conclusion, and since valid scientific evidence shows the applicability of various end-product tests to the use of the suture in humans, we believe that class II controls provide a reasonable means, consistent with the act's purpose, to regulate nonabsorbable polypropylene surgical suture.

SCIENTIFIC BASIS

Suture Characterization

By definition, the nonabsorbable polypropylene surgical suture is well characterized. The suture is a monofilament, nonabsorbable, sterile, flexible thread prepared from long-chain polyolefin polymer known as polypropylene and is indicated for use in soft tissue approximation. The polypropylene surgical suture meets USP requirements as described in the USP Monograph for Nonabsorbable Surgical Sutures; it may be undyed or dyed with an FDA approved color additive; and the suture may be provided with or without a standard needle attached.

The nonabsorbable polypropylene surgical suture manufacturing process begins with production of the isotatic form of the polypropylene polymer wherein the attached methyl groups are arranged in a stereoregular

configuration along one side of the "plane" described by a zig-zag carbon chain. It is produced in a solvent polymerization, using hydrocarbon solvent under pressure, at high temperatures and in the presence of a Zeigler-Natta catalyst which promotes the formation of the stereoregular isotatic form of the polypropylene polymer. The resulting insoluble isotatic polymer resin is subsequently purified by filtration and extraction to remove the catalyst, and then dried. Nonabsorbable polypropylene surgical suture may be left undyed (natural), or if desired, dyed with an FDA listed color additive in accordance with section 706 of the act.

The polypropylene resin is extruded at high temperature into polymer fibers of uniform diameter, and a specific multiple of their length are drawn or stretched to provide the necessary tensile properties. Nonabsorbable polypropylene surgical suture is ordinarily monofilamentous, and depending upon the final suture size desired, fibers of appropriate diameter and characteristics are produced. The processed thread is then cut to length, gauged to ensure uniform diameter and tensile strength in accordance with the requirements of United States Pharmacopeia (USP), appropriately packaged (with or without an attached needle), and sterilized to produce a finished suture (Refs. 7, 9, 29, 32, 65, 105, 133, 134 and 135).

Record data show that nonabsorbable polypropylene surgical suture's performance parameters and uses are well documented and understood, and that the generic type of device presents a reasonably uniform risk/benefit profile. Indeed the characteristics and composition of polypropylene are well-defined (Refs. 23, 24, 57, 58, 69, 72, 90, 91, 95, 113, 117, 120, 121, 126, 128-131, 134 and 135). Moreover, the performance parameters of existing nonabsorbable polypropylene surgical suture are well established (Refs. 9, 24, 29, 45, 50, 64, 121, 133, 134, 135 and 137) and the record shows the reasonably safe and effective use of nonabsorbable polypropylene surgical suture in humans (Refs. 17, 21, 33, 41, 42, 87, 95, 120 and 138).

The end product, given its indications for use, must have certain tensile strength characteristics (Refs. 9, 23, 28, 30, 34, 64, 74, 85, 89, 90, 91, 95, 113, 117, 120, 121, 126, 128, 129, 130, 133, 137 and 142). USP sutures, evaluated by uniform end-product testing, will perform successfully, notwithstanding different manufacturing processes (Refs. 7, 9, 64, 137, 24, 85, 133, 134 and 135), and will, among other things, have uniform tensile strengths. Since record data show that all nonabsorbable polypropylene surgical sutures present similar risks and performance characteristics (Refs. 9, 24, 29, 45, 50, 64, 121, 133, 134, 135 and 137), end product testing, in conjunction with other controls, will provide an appropriate means of reasonably assuring safe and effective nonabsorbable polypropylene surgical sutures.

In sum, the principal materials used to produce nonabsorbable polypropylene surgical suture is isotatic polypropylene polymer, and the physical characteristics of these polypropylene polymers are well understood. The USP Standard (Ref. 133 a-l), the American Society for Testing and Materials (ASTM) standards (Ref. 9 a-t) and other state-of-the-art test methods exist to evaluate and analyze the manufacturing process, composition, and physical, mechanical and biological properties of any nonabsorbable

polypropylene surgical suture (Refs. 28, 30, 34, 88, 92, 110, 112, 113, 116-119, 130, 132 and 138). Nonabsorbable polypropylene surgical sutures present the same risks and performance parameters and can be standardized by end-product tests, and are regulable by the same or similar controls. Accordingly, the record shows that nonabsorbable polypropylene surgical suture constitutes a well characterized generic type of device.

Control of Suture Performance

The parameters that need control to provide reasonable assurance of safety and effectiveness for nonabsorbable polypropylene surgical suture are suture breakage, tissue inflammatory response, infection, and suture-related calculogenesis. A discussion of each parameter and the appropriateness of a class II classification for nonabsorbable polypropylene surgical suture, as supported by valid scientific evidence, follows.

1. Suture Breakage

The most important function of a suture is to successfully hold tissue together until healing is sufficiently complete so as to negate the need of the suture. Failure of a suture prior to a wound regaining adequate strength may result in wound dehiscence: a disruption of apposed wound surfaces, interfering with the normal healing process. Suture breakage may occur where there is premature loss of tensile strength (Refs. 4, 23, 29, 32, 42, 43, 44, 64, 70, 83, 90, 95, 115, 117, 121, 126, 128, 129, 130 and 149), due to unfavorable physiological wound site conditions (Refs. 11, 17, 18, 22, 33, 48, 66, 68, 74, 79, 80, 87, 102, 121 and 137), poor surgical technique (Refs. 11, 21, 66, 74, 77, 80, 83, 102, 107, 108, 109, 115, 117, 121 and 137), or improper use of the suture (id.). Importantly, the cumulative risk of nonabsorbable polypropylene surgical suture breakage is small, and its ability to function properly is uncontested.

The data in the record reveal that the incidence of wound dehiscence varies according to a number of factors, not all of which relate to suture breakage (Refs. 11, 17, 18, 48, 54, 66, 68, 74, 80, 81, 87, 107, 108, 109, 121 and 137). Of those wounds that dehisce, only a small fraction are attributable to suture breakage (Refs. 11, 17, 22, 48, 66, 74, 79, 109 and 121). It has also been shown that the incidence of wound dehiscence due to suture breakage occurs infrequently with nonabsorbable polypropylene surgical suture (Refs. 11, 22, 66, 74, 79, 108 and 109), and that the overall incidence of wound dehiscence with nonabsorbable polypropylene surgical suture is low (Refs. 22, 41, 68, 74, 79, 87 and 109).

The loss of tensile strength leading to suture breakage is a potential cause of failure of nonabsorbable polypropylene surgical suture in certain applications (Refs. 4, 32, 42, 70, 115 and 149). Retention of the suture's tensile strength is critical to the function of nonabsorbable polypropylene surgical suture. The record data show that the loss of tensile strength in vivo is primarily related to the oxidative degradation of the polypropylene polymer (Refs. 4, 29, 32, 42, 43 and 44) and that the polymer's degradation proceeds slowly and is generally not considered clinically significant under most circumstances of use (Refs. 1, 4, 42, 121 and 149). The rate and extent

of oxidative degradation vary according to exposure to ultraviolet radiation, and may make the use of the suture in the eye questionable (Refs. 4, 32, 42, 70 and 149). Oxidative enzyme activity and the type of tissue at the wound site, e.g., actively metabolizing tissues, tissues with high oxygen concentration, and inflammation may also contraindicate the suture for certain applications (Refs. 4, 32, 42, 43, 44, 70 and 149).

The patient's health and response to the suture material may affect wound healing (Refs. 11, 17, 18, 48, 66, 74, 80, 81, 87, 107, 108, 109 and 121). Patients whose health has been compromised or weakened by poor nutrition, advanced age, obesity, uncontrolled diabetes, infection, anemia, or with certain forms of cancer, may exhibit delayed wound healing (Refs. 11, 17, 18, 48, 66, 74, 80, 81, 87, 107, 108, 109 and 121) which may increase the likelihood of suture failure. Although some of these factors have been shown experimentally to delay increases in wound strength, a nonabsorbable suture, such as nonabsorbable polypropylene surgical suture, may be preferred over absorbable sutures due to the suture's continuous support of tissues (Refs. 17, 48, 66, 74, 108, 121 and 137).

The appropriate use of nonabsorbable polypropylene surgical suture is important in defining its performance. The record shows that nonabsorbable polypropylene surgical suture has been successfully used in various wound sites and conditions in humans (Refs. 17, 21, 33, 41, 42, 87, 95, 120 and 138). Although, wound dehiscence is most significant in wound closures involving sites which can undergo expansion, stretching, or distention, such as the abdomen, chest, and joints, nonabsorbable polypropylene surgical suture may be the suture of choice due to its continued support of tissues (Refs. 11, 17, 18, 22, 33, 48, 66, 74, 79, 80, 81, 87, 102, 108, 121 and 137). Using nonabsorbable polypropylene surgical suture to close certain wounds has documented advantages related to the physical properties of the suture (Refs. 11, 22, 33, 66, 74, 79, 80, 81, 87, 108 and 121).

Surgical technique also affects the performance of sutures, including nonabsorbable polypropylene surgical suture. Improper closure technique can result in tissue separation and failure of the wound to heal. The factors relating to the wound closure technique that contribute to wound dehiscence include the tightness with which sutures are tied, suture knot security, the adequacy of tissue bites to allow for adequate wound expansion due to distention and damage to the suture during placement (Refs. 11, 17, 18, 21, 23, 48, 57, 58, 64, 66, 69, 74, 77, 79, 83, 87, 95, 102, 107, 108, 109, 115, 117, 120, 121, 129 and 130).

The critical parameter of tensile strength can be controlled by standard in vitro test methods and animal testing. The tensile strength of nonabsorbable polypropylene surgical suture before implantation and after explantation may be measured in a motor-driven tensile strength machine using equipment and procedures described in the USP (Refs. 133, 134 and 135). Moreover, various American Society for Testing and Material (ASTM) tests to evaluate suture strength exist and include, for example, yarn breaking load, breaking tenacity in loop/knot configuration, single textile fiber tensile strength, and in vitro strength loss and material degradation tests (Refs. 9, 134 and 135). Finally, to determine the effects of implantation of

nonabsorbable polypropylene surgical suture upon tensile strength, various in vitro and in vivo methods used by Salthouse (Refs. 116 and 117), Postlethwait (Ref. 110), and others (Refs. 30, 64, 128, 129 and 130), which compare the tensile strength of various absorbable and nonabsorbable sutures, show a suture's performance characteristics.

The various evaluative methods included in the above references are applicable to the safe and effective use of nonabsorbable polypropylene surgical suture in humans in that sutures that have been successfully used in humans are routinely evaluated with these evaluative methods (Refs. 17, 21, 33, 41, 42, 87, 95, 120 and 138). Importantly, the time necessary for wound healing in various sites in humans is known (Refs. 2, 3, 5, 6, 13, 14, 19, 20, 24, 25, 27, 38, 39, 49, 50, 52, 60, 61, 63, 74, 75, 76, 77, 78, 98, 101, 103, 107, 114, 116, 121, 124, 127, 137 and 143), and the above methods permit a determination of whether sufficient suture tensile strength will be present over time to assure a successful result at any given wound site.

Also, many of the above-identified performance parameters and risks can be adequately controlled by labeling disclosures which may be incorporated into a class II standard or required by the class I misbranding controls, which include, among other things, the requirement of adequate directions for use. Disclosures can be made which contain warnings against the use of nonabsorbable polypropylene surgical suture in certain conditions, such as intracamerally in the eye. Also, risks may be avoided by disclosing in labeling that users must be familiar with surgical procedures and techniques involving nonabsorbable polypropylene surgical suture before using it to close wounds.

2. Tissue Inflammatory Response

A tissue inflammatory response is an acute or chronic, localized reaction. Many factors may cause a tissue inflammatory response, including trauma attributed to the implantation of a suture, (Refs. 17, 29, 50, 66, 89, 110, 116, 117, 121, 125, 126 and 137), and foreign body reactions to the suture material (Ref. 74, 87, 107, 119, 121, and 123).

Various studies have documented that an early tissue inflammatory reaction results from the trauma of inserting sutures and does not occur as a result of a reaction to suture material (Refs. 82, 84 and 144). When the suture is placed within tissue with little or no trauma, no inflammatory cell response results, suggesting the conclusion that the body's nonspecific response to tissue injury induces the appearance of inflammatory cells usually seen immediately after suturing (Refs. 31, 87, 107, 119, 146 and 147). The initial reaction of tissues after suturing reflects the amount of injury inherent in the process, and that injury typically is the same for all sutures 5 to 7 days after suturing (Refs. 17, 111, 121, 126, 127 and 137).

The inflammatory response observed beyond 5 to 7 days postoperatively is dependent upon the nature of the specific suture material employed. Specifically, synthetic materials elicit a lesser response than sutures of natural origin (Refs. 29, 110, 116, 117, 119, 121 and 136), and nonabsorbable polypropylene surgical sutures elicit a milder response than absorbable

sutures (Refs. 37, 89, 119, 126, 127 and 137). Additionally, fine gauge sutures provoke a lesser response than large diameter sutures because of their lesser mass and therefore lesser amount of implanted foreign material (Refs. 50 and 136).

Record data show that nonabsorbable polypropylene surgical suture elicits a very mild chronic inflammatory response (Refs. 29, 89, 110, 116, 117, 119, 121, 126, 127 and 137), and because it is ordinarily monofilmentous, this response is among the most benign elicited by any suture material (Ref. 110). Following the initial inflammatory phase, a mild chronic tissue response to nonabsorbable polypropylene surgical suture is seen which is typically characterized by gradual formation of a fibrous encapsulation of the suture with little or no persistent cellular response (Refs. 87, 107, 119, 146 and 147). The chronic tissue inflammatory response to nonabsorbable polypropylene surgical suture is observed to be mild, and less than that elicited by certain other sutures (Refs. 87, 107, 119, 146 and 147) even though the chronic inflammatory response to nonabsorbable polypropylene surgical suture may be associated with granuloma formation in certain circumstances and wound sites (Refs. 74, 87, 107, 119, 121 and 123).

Because of the biocompatability of the synthetic polypropylene material, nonabsorbable polypropylene surgical suture has not been associated with allergic and antigenic reactions. Although the manufacturing process may introduce impurities and residues that can cause tissue inflammatory response, numerous well-established biocompatibility tests provide methods to evaluate a suture's inflammatory potential, including USP tests for impurities and residues, or other state-of-the-art analytical methods (Refs. 8, 9, 10, 12, 51, 53, 62, 65, 72, 86, 93, 96, 97, 104, 106, 112, 132, 133, 134, 145 and 148).

In summary, the risk of early tissue inflammation resulting from trauma is related to the user technique and is no greater for nonabsorbable polypropylene surgical suture than for other suture material. Further, the foreign body response to nonabsorbable polypropylene surgical suture is mild in nature and, therefore, the suture in some circumstances may be preferred to other nonabsorbable sutures. Appropriate labeling disclosures related to tissue inflammation may indicate that all nonabsorbable sutures present an inflammatory response and that nonabsorbable polypropylene surgical suture is less pronounced than that of other nonabsorbable sutures. Moreover, to the extent the manufacturing process may cause residues that introduce a potential for allergic or antigenic reaction, which otherwise is not present with the nonabsorbable polypropylene surgical suture, well-established biocompatibility tests, as part of a standard, exist to evaluate the suture's inflammatory potential.

3. Infection

Although polypropylene surgical suture is manufactured and marketed as a sterile device in accordance with voluntary standards for sterility (Refs. 7, 9, 133 and 134), it, nonetheless, may exacerbate the effects of an existing wound infection, because of its composition, physical configuration, and duration of contact with tissue (Refs. 15, 16, 29, 31, 35, 36, 40, 45, 48, 50,

55, 56, 66, 73, 122, 123, 125, 127 and 141). It has been established that the presence of suture material in a wound increases the wound's susceptibility to infection where the suture serves as a conduit for the mechanical transport of bacteria (Refs. 15, 29, 31, 36, 40, 50, 55, 66, 73, 108, 123, 125, 127, 136 and 139). Also, materials which permit the adherence of the largest amount of bacteria cause the greatest degree of post-surgical infection (Refs. 31, 36, 56, 73 and 125). Indeed, a comparative study of 10 sutures demonstrates that the physical configuration and chemical nature of various suture materials, their coating mechanisms, and the duration of contact between the sutures and bacteria, contribute to the bacterial adherence of the suture (Ref. 31). The physical configuration of suture material is found to correlate positively with the degree to which sutures aggravate infected wounds (id.), and the use of suture coatings do not appear to reduce the suture-related infection rate (Refs. 36, 45, 50, 55, 123 and 127).

In the presence of infection or contamination, all sutures appear to potentiate the wound infection (Refs. 29, 45, 48, 50, 123 and 127). While nonabsorbable polypropylene surgical suture is not unique in its potential to exacerbate infection, it does appear to carry a somewhat lesser risk than other sutures in this regard (Refs. 16, 32, 40, 55, 95, 121, 123, 126, 138 and 170). The choice of suture material may, therefore, be critical when closing a wound in the presence of infection or potential infection. Because the nonabsorbable polypropylene surgical suture presents somewhat of a lesser risk than other sutures to potential infection, it is a suture of choice for infected wounds or contaminated wounds that present a substantial risk of infection (Refs. 16, 29, 32, 35, 40, 45, 48, 55, 73, 95, 123, 126, 138, 139, 140 and 141).

In summary, since suture selection may be a critical factor in avoiding the exacerbation of an infection, adequate labeling for the nonabsorbable polypropylene surgical suture, as part of a standard, could state that it is a suture of choice in closing infected or contaminated wounds.

4. Calculogenesis

Nonabsorbable polypropylene surgical suture, like other suture material, has been shown to be a nidus for calculogenesis when in contact with salt solutions of the bladder and biliary tract (Refs. 47, 66, 107 and 137). Calculi formation occurs on other natural and synthetic sutures in the bladder, and calculi formation appears to be dependant on the length of time the suture is in contact with urine in the bladder (Refs. 18, 47, 107, 117, and 137). Studies also report that nonabsorbable polypropylene surgical suture, and other sutures, when exposed to salt solutions in the common bile duct have been associated with stone formation (Refs. 18, 60 and 137).

The risk of calculogenesis resulting from implantation of nonabsorbable polypropylene surgical suture in either the urinary or biliary tract is related to the length of time the suture is in contact with a salt solution in those tracts. The risk of calculogenesis with nonabsorbable polypropylene surgical suture is typical of that associated with all nonabsorbable sutures. Thus, adequate labeling as part of a standard, can control this risk by stating that it is inadvisable to place nonabsorbable polypropylene surgical

suture, or for that matter, any suture, in contact with salt solutions in the body's urinary and biliary tracts.

Based on the information presented above, it can be concluded that nonabsorbable polypropylene surgical suture is well characterized and that there is sufficient publicly available valid scientific evidence to demonstrate that a performance standard can be established and used, in combination with the general controls, to provide reasonable assurance of the safety and effectiveness of nonabsorbable polypropylene surgical suture. For control of suture breakage, in particular, for control of suture tensile strength, a standard can assure device safety and effectiveness. See pages 8-9. Likewise, suture-related tissue inflammatory response can be controlled by a performance standard. See page 10.

The act's general controls also make a substantial contribution to the regulation of nonabsorbable polypropylene surgical suture. Manufacturing processes for nonabsorbable polypropylene surgical suture are and will be subject to FDA's Good Manufacturing Practice regulations, and the act's adulteration provisions. Moreover, labeling warnings and disclosures identified throughout this order will provide sufficient control of various nonabsorbable polypropylene surgical suture-related performance parameters or risks to reasonably assure the suture's safe and effective use.

PRIORITY FOR THE DEVELOPMENT OF A STANDARD

While valid scientific evidence demonstrates that a performance standard may be written to control the material, composition, and physical characteristic of this generic type of device in order to reasonably assure its safety and effectiveness, one is not immediately needed. Existing devices, within the generic type covered by this order, typically conform to voluntary standards, including USP standards for nonabsorbable surgical suture. Moreover, nonabsorbable polypropylene surgical suture, as currently manufactured, has established a reasonable record of safe and effective use. The basic properties, principles of manufacture, and appropriate indications and contra-indications for use of nonabsorbable polypropylene surgical suture are well-established, both scientifically and clinically, as documented in publicly available information contained in the petition (Refs. 28, 39, 63, 64, 75, 76, 90, 98, 107, 121, 126 and 134).

In this matter, significant publicly available information indicates that existing nonabsorbable polypropylene surgical sutures are generally safe and effective (Refs. 24, 29, 39, 63, 75, 76, 80, 85, 98, 107, 110, 117, 121 and 127). Thus, FDA concludes that development of a mandatory performance standard is not immediately necessary to protect the public health.

State-of-the-art test methods are well-established to evaluate and analyze the structure, composition, physical, chemical, mechanical, physicochemical and biological properties of any nonabsorbable polypropylene surgical suture to allow a precise determination to be made of the relative safety and effectiveness of marketed nonabsorbable polypropylene surgical sutures and those intended for commercial distribution. Thus, the determination of

comparable safety and effectiveness of future nonabsorbable polypropylene surgical suture and marketed sutures can be made in the context of a premarket notification under section 510(k) of the act, 21 USC 360(k).

FDA, therefore, respectfully disagrees with Panel's recommendation that the promulgation of a mandatory performance standard be a high priority. FDA concludes that development of a mandatory performance standard should be a low priority because the establishment of a regulatory standard is not immediately necessary to protect the public health.

CONCLUSION

Based on the information provided in the petition and presented at the panel meeting, and the information submitted to the administrative record, FDA concludes that the generic type of device, nonabsorbable polypropylene surgical suture, should be reclassified from class III to class II with a low priority for the development of a performance standard.

Sincerely yours,

Robert L. Sheridan
Director
Office of Device Evaluation
Center for Devices
and Radiological Health

Enclosure: References

cc: Howard R. Asher
President
Advanced Biosearch Associates
3880 Blackhawk Road
Danville, California 94526-4617

Enclosure

REFERENCES FOR NONABSORBABLE POLYPROPYLENE SURGICAL SUTURE

1. Allen MV, Jones Ed, Snow R, et al: Long-term study of iris sutures in rabbits. Ophthalmic Surg 13(9):733-6, Sep 1982

2. Amshel AL: The use of vicryl (Polyglactin 910) sutures in colonic and rectal surgery. Dis Colon Rectum 20(7):636-8, Oct 1977

3. Andersen JR, et al.: Polyglycolic acid, silk, and topical ampicillin. Arch Surg 115:293-5, Mar 1980

4. Apple DJ, Mamalis N, Brady SE, et al: Biocompatibility of implant materials: A review of scanning electron microscopic study. Am Intra-Ocular Implant Soc J 10:53-65, 1984

5. Apt L, Gaffney WL, Dora AF: Experimental suture studies in strabismus surgery. II. Comparison of tensile strength of plain catgut with polyglycolic acid (Dexon) sutures after extraocular muscle surgery. Albrecht von Graefes. Klin Arch Ophthalmol 201:19-27, 1976

6. Assimos DG, et al.: Efficacy of polyglycolic acid (PGA) tubing stents in ureteroureterostomies. Urol Res 12:291-3, 1984

7. Association for the Advancement of Medical Instrumentation: Guideline for industrial ethylene oxide sterilization for medical devices. AAMI ST27-P-11/87, pp 1-76, Nov 1987

8. General Plastic Surgery Device Panel's Meeting Transcript, Thursday, October 20, 1988.

9. American Society for Testing and Materials Standards:

a.	#D	204-82	Standard Methods of Testing Sewing Threads
b.	#D	1423-82	Standard Method of Testing for Twist in Yarns by the Direct-Counting Method
c.	#D	1774-79	Standard Test Methods for Elastic Properties of Textile Fibers
d.	#D	2101-82	Standard Test Methods for Tensile Properties of Single Man-Made Textile Fibers Taken From Yarns and Tows
e.	#D	2256-80	Standard Test Method for Breaking Load (Strength) and Elongation of Yarn by the Single Strand Method
f.	#D	2257-80	Standard Test Method for Extractable Matter in Yarns
g.	#D	2259-85	Standard Test Methods for Shrinkage of Yarns in Boiling Water or Dry Heat
h.	#D	3217-79	Standard Test Methods for Breaking Tenacity of Man-Made Textile Fibers in Loop or Knot

			Configurations
i.	#D	3412-86	Standard Test Methods for Coefficient of Friction, Yarn to Yarn
j.	#D	3822-82	Standard Test Method for Tensile Properties of Single Textile Fibers
k.	#F	469-78	Standard Practice for Assessment of Compatibility of Nonporous Polymeric Materials for Surgical Implants With Regard to Effect of Materials on Tissue
l.	#F	719-81	Standard Practice for Testing Biomaterials in Rabbits for Primary Skin Irritation
m.	#F	720-81	Standard Practice for Testing Guinea Pigs for Contact Allergens: Guinea Pig Maximization Test
n.	#F	748-82	Standard Practice for Selecting Generic Biological Test Methods for Materials an Devices
o.	#F	749-82	Standard Practice for Evaluating Material Extracts by Intracutaneous Injection the Rabbit
p.	#F	750-82	Standard Practice for Evaluating Material Extracts by Systematic Injection in the Mouse
q.	#F	756-82	Standard Practice for Assessment of Hemolytic Properties of Materials
r.	#F	763-82	Standard Practice for Short-Term Screening of Implant Materials
s.	#F	813-83	Standard Practices for Direct Contact Cell Culture Evaluation of Materials for Medical Devices
t.	#F	895-84	Standard Test Method for Agar Diffusion Cell Culture Screening for Cytotoxicity

10. Autian J: Testing for toxicity. In von Recum AS (ed): Handbook of biomaterials evaluation. New York, Macmillan Co (15):167-178, 1986.

11. Baggish MS, Lee WK: Abdominal wound disruption. Obstet Gynecol 46(5):530-4, Nov 1975

12. Barenberg SA, et al.: Structural and chemical characterization of polymers. In Techniques of biocompatibility testing. Williams DF (ed): Boca Raton, CRC Press 2(1):1-47, 1986

13. Bartone FF, Gardner PJ, Hutson JC: Polyglactin 910 suture in urinary tract. Urology 9(5):521-5, May 1977

14. Bartone FF, Shires TK: The reaction of kidney and bladder tissue to catgut and reconstituted collagen sutures. Surg Gynecol Obstet, Jun 1969, pp 1221-5

15. Blomstedt B, Osterberg B: Fluid absorption and capillarity of suture materials. Acta Chir Scand 143(2):67-70, 1977

16. Bridgens NK: A comparative study of surgical suture materials and closure techniques. J AOA 82(9):715/37-718/40, May 1983

17. Bucknall TE: Factors affecting healing. In Wound healing for surgeons. Bucknall TE, Ellis H (eds). Philadelphia, Bailliere Tindall (3):42-74, 1984

18. Bucknall TE: Wound healing in abdominal operations. Surg Ann 17:1-22, 1985

19. Burcharth F, et al.: Inguinal hernia repair with silk or polyglycolic acid sutures. A controlled trial with 5 years follow up. World J Surg 7(3):446-8, May 1983

20. Cabaud HE, Feagin JA, Rodkey WG: Acute anterior cruciate ligament injury and repair reinforced with a biodegradable intraarticular ligament. Am J Sports Med 10(5):259-65, 1982

21. Calhoun TR, Kitten CM: Polypropylene suture - Is it safe? J Vasc Surg 4(1):98-100, July 1986

22. Cameron AEP, Gray RCF, Talbot RW, et al: Abdominal wound closure: a trial of Prolene and Dexon. Br J Surg 67:487-8, 1980

23. Campbell JR, Marks A: Suture materials and suturing techniques. In Pract 7(3):72-5, May 1985

24. Capperauld I, Bucknall TE: Sutures and Dressings. In wound healing for surgeons. Bucknall TE, Ellis H (eds). Philadelphia, Bailliere Tindall pp 75-93, 1984

25. Case CD, Glenn JF, Postlethwait RW: Comparison of absorbable sutures in urinary bladder. Urology 7(2):165-8, Feb 1976

26. Casey DJ, Lewis OG: Absorbable and Nonabsorbable Suture. In Handbook of Biomaterials Evaluation: Scientific, Technical, and Clinical Testing of Implant Materials. vonRecum AF: New York, Macmillan Publishing Company, ch 7 pp 86-94, 1986

27. Cassie AB: Suture materials and the healing of surgical wounds. In Operative surgery and management. Keen G (ed): Wright PSG, Bristol pp 1-8, 1981

28. Chu CC: Mechanical properties of suture materials. An important characterization. Ann Surg 193(3):365-71, Mar 1981

29. Chu CC: The degradation and biocompatibility of suture materials. In CRC Critical Review in Biocompatibility. Williams DR (ed): ed 3, CRC Press, Boca Raton, FL, vol 1, issue 3, p 261-322, 1985

30. Chu CC, Moncrief G: An in vitro evaluation of the stability of mechanical properties of surgical suture materials in various pH conditions. Ann Surg 198(2):223-8, Aug 1983

31. Chu CC, Williams DF: Effects of physical configuration and chemical structure of suture materials on bacterial adhesion. A possible link to wound infection. Am J Surg 147:197-204, Feb 1984

32. Clayman HM: Polypropylene. Ophthalmology 88(9):959-64, Sep 1981

33. Corman ML, Veidenheimer MC, Coller JA: Controlled clinical trial of three suture materials for abdominal wall closure after bowel operations. Am J Surg 141:510-3, Apr 1981

34. Dahlke H, Dociu N, Thurau K: Thrombogenicity of different suture materials as revealed by scanning electron microscopy. J Biomed Mater Res 14:251-68, 1980

35. Dardik H, Dardik I, Laufman H: Clinical use of polyglycolic acid polymer as a new absorbable synthetic suture. Am J Surg 121:656-60, Jun 1971

36. de Holl D, Rodeheaver G, Edgerton MT, et al: Potentiation of infection by suture closure of dead space. Am J Surg 127:716-20, Jun 1974

37. Delbeke LO, Gomel V, McComb PF, et al: Histologic reaction to four synthetic microsutures in the rabbit. Fertil Steril 40(2):248-52, Aug 1983

38. Deveney KE, Way LW: Effect of different absorbable sutures on healing of intestinal anastomoses. Am J Surg 133:86-93, Jan 1977

39. Deveney and Dunphy: Wound healing in the gastrointestinal tract. In Fundamentals of wound management. Hunt TK, Dunphy JE (eds): Appleton-Century-Crofts, New York, pp 569-593, 1979

40. Dineen P: The effect of suture material in the development of vascular infection. From the Surgical Bacteriology Research Laboratory, Department of Surgery, The New York Hospital-Cornell Medical Center

41. Donaldson DR, Zoltowski JA, Guillou PJ, et al: Does the type of suture material contribute to the strength of the lateral paramedian incision? Br J Surg 69:163-5, 1982

42. Drews RC: Polypropylene in the human eye. Am Intra-Ocular Implant Soc J 9:137-42, Spring 1983

43. Drews RC: Lens implantation: Lessons learned from the first million. Trans Ophthalmol Soc UK 102:505-9, 1982

44. Drews RC: Quality control, and changing indications for lens implantation. Am Acad Ophthalmol 90(4):301-10, Apr 1983

45. Edlich RF, Panek PH, Rodeheaver GT, et al: Physical and chemical configuration of sutures in the development of surgical infection. Ann Surg 177(6):679-88, Jun 1973

46. Edlich RF, Panek PH, Rodeheaver GT, et al: Surgical sutures and infection: A biomaterial evaluation. J Biomed Mater Res Symposium 5:115-26, 1974

47. Edlich RF, Rodeheaver GT, Thacker JG: Considerations in the choice of sutures for wound closure of the genitourinary tract. J Urol 137:373-9, Mar 1987

48. Ellis H: The abdominal wall. In Wound healing for surgeons. Bucknall TE, Ellis H (eds). Philadelphia, Balliere Tindall (7):124-142, 1984

49. Ethicon Inc.: Wound closure manual, 1985

50. Forrester JC: Sutures and sepsis. In Controversies in Surgical Sepsis. Karran S (ed): Praeger, ch 5, pp 43-52, 1980

51. Forster R: Mutagenicity testing and biomaterials. In Techniques of biocompatibility testing.Williams DF (ed): Boca Raton, CRC Press 2(7):137-149, 1986

52. Francois J, Verbraeken J: Polyglycolic acid suture in retinal detachment surgery. Ophthalmologica 174:277-9, 1977

53. Freeman WJ: Characterization of Polymers. In Encyclopedia of Polymer Science & Engineering. Mark HF, et al. (eds). J Wiley & Sons, New York, pp 290-327, 1985

54. Gallitano AL, Kondi ES: The superiority of polyglycolic acid sutures for closure of abdominal incisions. Surg Gynecol Obstet 137:794-6, Nov 1973

55. Georgiade GS: Wound contamination. Postgrad Med 73(3):247-54, Mar 1983

56. Gristina AG, Price JL, Hobgood CD, et al: Bacterial colonization of percutaneous sutures. Surgery 98(1):12-9, Jul 1985

57. Gupta BS, Wolf KW, Postlethwait RW: Effect of suture material and construction on frictional properties of sutures. Surg Gynecol Obstet 161:12-6, Jul 1985

58. Gupta BS, Wolf KW, Postlethwait RW: Effect of lubrication on frictional properties of sutures. Surg Gynecol Obstet 161:416-8, Nov 1985

59. Hastings JC, Van Winkle W, Barker E, et al: Effect of suture materials on healing wounds of the stomach and colon. Surg Gynecol Obstet 140:701-7, May 1975

60. Hastings JC, Van Winkle W, Barker E, et al: The effect of suture materials on healing wounds of the bladder. Surg Gynecol Obstet 140:933-7, Jun 1975

61. Hastings JC, et al.: The effect of suture materials on healing wounds of the bladder. Surg Gynecol Obstet 140:933-7, June 1975

62. Henry TJ (ed): Guidelines for the preclinical safety evaluation of materials used in medical devices. HIMA Report 85(1), 1985

63. Heppenstall: Fracture and Cartilage. In Fundamentals of wound management. Hunt TK, Dunhy JE (eds): Appleton-Century-Crofts, New York, pp 524-551, 1979

64. Herrmann JB: Tensile strength and knot security of surgical suture materials. Am Surg pp. 209-17, Apr 1971

65. HIMA guidelines for the analysis of ethylene oxide residues in medical devices, 1980

66. Hunt TK: Wound complications. In Management of Surgical Complications, Artz CP, Hardy JD (eds): ed 3, Philadelphia, W.B. Saunders Co, ch 2, pp 21-32, 1975

67. IMS America Ltd: Total polypropylene suture sales in the United States for 1986 and 1987

68. Irvin TT, Koffman CT, Duthie HL: Layer closure of laparotomy wounds with absorbable and nonabsorbable suture materials. Br J Surg 63:793-6, 1976

69. Johnson CD: Two alternative methods for tying the surgeon's knot with one hand. Surg Gynecol Obstet 164:375-6, Apr 1987

70. Jongebloed WL, Figueras MJ, Humalda D, et al: Mechanical and biochemical effects of man-made fibres and metals in the human eye, a SEM-study. Doc Ophthalmol 61:303-12, 1986

71. Kaminski JM, Katz AR, Woodward SC: Urinary bladder calculus formation on sutures in rabbits, cats and dogs. Surg Gynecol Obstet 146:353-7, Mar 1978

72. Kampf G: Characterization of plastics by physical methods. Experimental techniques and practical application. Hanser Publishers, New York, 1986

73. Katz S, Izhar M, Mirelman D: Bacterial adherence to surgical sutures. A possible factor in suture induced infection. Ann Surg 194(1):35-41, Jul 1981

74. Kenady DE: Management of abdominal wounds. Surg Clin North Am 64(4):803-7, Aug 1984

75. Ketchum: Peripheral nerve repair. In Fundamentals of wound management. Hunt TK, Dunphy JE (eds): Appleton-Century-Crofts, New York, pp 450-475, 1979

76. Ketchum: Tendon healing. In Fundamentals of wound management. Hunt TK, Dunphy JE (eds): Appleton-Century-Crofts, New York, pp 500-523, 1979

77. Ketchum LD: Suture materials and suture techniques used in tendon repair. Hand Clin 1(1):43-53, Feb 1985

78. Kleener J: Filtration blebs in corneoscleral wounds sutured with Dexon 7-0 and Dexon 8-0. Acta Ophthalmol 58:957-62, 1980

79. Knight CD, Griffen FD: Abdominal wound closure with a continuous monofilament polypropylene suture. Experience with 1,000 consecutive cases. Arch Surg 118:1305-8, Nov 1983

80. Kon ND, Meredith JW, Poole GV, et al: Abdominal wound closure. A comparison of polydioxanone, polypropylene, and Teflon -coated braided Dacron sutures. Am Surg 50(10):549-51, Oct 1984

81. Konigsberg HA, Presto AJ, Marshall VF: Wound dehiscence in urological patients. J Urol 114:578-80, Oct 1975

82. Kraissl CJ, Kesten BM, Cimiotti JG: The relation of catgut sensitivity to wound healing. Surg Gynecol Obstet 66:628-636, 1938

83. Landymore RW, Marble AE, Cameron CA: Effect of force on anastomotic suture line disruption after carotid arteriotomy. Am J Surg 154:309-12, Sep 1987

84. Langston HT: The problem of catgut sensitivity and its relation to wound healing. Ann Surg 115:141, 1942

85. Lee S, Hailey DM, Lea AR: Tensile strength requirements for sutures. J Pharm Pharmacol 35:65-9, 1983

86. Lifshin E, Williams EA: Analytical methods. In Encyclopedia of Chemical Technology. Mark HF, et al. (eds) J Wiley & Sons, New York, pp 586-683, 1978

87. LoCicero J III, Robbins JA, Webb WR: Complications following abdominal fascial closures using various nonabsorbable sutures. Surg Gynecol Obstet 157(1):25-7, Jul 1983

88. Magnusson B, Kligman AM: The identification of contact allergans by animal assay: The guinea pig maximization test. J Invest Dermat 52(3):268-276, 1969

89. Macht SD, Krizek TJ: Sutures and suturing - current concepts. J Oral Surg 36:710-2, Sep 1978

90. Marchant LH: Effect of elongation rate on tensile strength of surgical suture materials. Surg Gynecol Obstet 138(2):231-3, 1974

91. Marchant LH, Knapp S, Braun H, et al: Effect of elongation rate on the percentage elongation of surgical suture material. Surg Gynecol Obstet 139:389-91, Sep 1974

92. Marzulli F, Maguire HC: Usefulness and limitations of various guinea-pig tests for skin hypersensitivity. Food Chem Toxicol 20:67-74, 1982

93. Merritt K: Hypersensitivity induction. In Handbook of biomaterials evaluation. von Recum AS (ed): New York, Macmillan Co. (16):179-187, 1986

94. Merritt K: Immunological testing of biomaterials. In Techniques of biocompatibility testing. Williams DF (ed). CRC Press, Boca Raton, Fl., 2(6):123-136, 1986

95. Miller JM, Kimmel LE: Clinical evaluation of monofilament polypropylene suture. Am Surg 33(8):666-70, Aug 1967

96. Mitchell J Jr (ed): Applied polymer analysis and characterization. Hanser Publishers, New York, 1987

97. Mitchell J Jr: Chemical Analysis. In Encyclopedia of Polymer Science & Engineering. Mark HF, et al. (eds). J Wiley & Sons, New York, pp 381-420, 1985

98. Moore and Malone: Vascular repair. In Fundamentals of wound management. Hunt TK, Dunphy JE (eds): Appleton-Century-Crofts, New York, pp. 476-499, 1979

99. Morris MC, Baquero A, eEdovan, et al: Urolithiasis on absorbable and non-absorbable suture materials in the rabbit bladder. J Urol 135:602-3, 1986

100. Mowbray SL, Chang SH, Casella JF: Estimation of the useful lifetime of polypropylene fiber in the anterior chamber. Am Intra-Ocular Implant Soc J 9:143-7, Spring 1983

101. Munton CGF, et al.: Vicryl (Polyglactin 910): A new synthetic absorbable suture in ophthalmic surgery. A preliminary study. Br J Ophthalmol 58:941-7, 1974

102. Myhre OA: Correspondence. Breakage of prolene suture. [Letter to the editor.] Am Thorac Surg ____:121, _____

103. Nachemson A, Nordwall A: Wound strength in a clinical material. Scand J Plast Reconstr Surg 9:93-7, 1975

104. Northrup SJ: Mammalian cell culture models. In Handbook of biomaterials evaluation. von Recum AS (ed). New York, Macmillan Co. (19)209-225, 1988

105. Official Monograph for Nonabsorbable Surgical Sutures. In The United States Pharmacopeia, XXI, 21st Revision, pp 1007-1009, 1156-1160 and 1274-1275, 1985 and Fourth Supplement, pp 2225-2226, November 1986

106. Paynter RW: Surface analytical techniques in biomaterials development. In Techniques of biocompatibility testing. Williams DF (ed): Bocat Raton, CRC Press 2(2):49-80, 1986

107. Peacock EE Jr (ed): Wound Repair. ed 3, Philadelphia, W.B. Saunders Company, 1984

108. Pellegrini CA: Postoperative complications. In Current Surgical Diagnosis & Treatment.Way LW (ed): ed 7, Los Altos, CA, Lange Medical Publications, ch 4, pp 23-5, 1985

109. Poole GV, Meredith JW, Kon ND, et al: Suture technique and wound-bursting strength. Am Surg 50(10):569-72, Oct 1984

110. Postlethwait RW: Long-term comparative study of nonabsorbable sutures. Ann Surg 171(6):892-8, 1970

111. Postlethwait RW: Principals of operative surgery: Antisepsis, technique, sutures, and drains. In Davis-Christopher textbook of surgery. The biological basis of modern surgical practice, 12th ed. Sabiston DC (ed), W.D. Saunders Co., Philadelphia, pp 317-332, 1981

112. Rae T: Tissue culture techniques in biocompatibility testing. In Techniques of biocompatibility testing. Williams DF (ed): Boca Raton, CRC Press 2(3):81-93, 1986

113. Rodeheaver GT, Borzelleca DC, Thacker JG, et al: Unique performance characteristics of Novafil . Surg Gynecol Obstet 164:230-6, Mar 1987

114. Ross G, Pavlides C, Long F, et al: Absorbable suture materials for vascular anastomoses. Tensile strength and axial pressure studies using polyglycolic acid sutures. Am Surg 47(12):541-7, Dec 1981

115. Roy J, Guidoin R, Cardou A, et al: Cardiovascular sutures as assessed by scanning electron microscopy. Scanning Electron Microscopy 3:203-10, 1980

116. Salthouse TN: Biologic response to sutures. Otolaryngol Head Neck Surg 88:658-64, Nov-Dec 1980

117. Salthouse TN: Tissue response to sutures. In Biomaterials in Reconstructive Surgery. Rubin LR (ed): ch 13, pp 131-41, 1983

118. Salthouse TN, Matlaga BF: An approach to the numerical quantitation of acute tissue response to biomaterials. Biomat Med Dev Art Org 3(1):47-56, 1975

119. Salthouse TN, Matlaga BF, Wykoff MH: Comparative tissue response to six suture materials in rabbit cornea, sclera, and ocular muscle. Am J Ophthalmol 84(2):224-33, Aug 1977

120. Sanders RJ: A new monofilament polypropylene suture. Exp Med Surg 28:224-7, 1970

121. Sanz L, Smith S: Mechanisms of wound healing, suture material, and wound closure. In Strategies in Gynecological Surgery. Buchsbaum HJ, Walton LA (eds): New York, Springer-Verlag, ch 5, pp 53-75, 1986

122. Scher KS, Bernstein JM, Jones CW: Infectivity of vascular sutures. Am Surg 51(10):577-79, Oct 1985

123. Sharp WV, Belden TA, King PH, et al: Suture resistance to infection. Surgery 91(1):61-3, Jan 1982

124. Stephenson KL: Suturing. Surg Clin North Am 57(5):863-73, Oct 1977

125. Sugarman B, Musher D: In vitro adherence of bacteria to suture materials. Clin Res 28(5):832A, 1981

126. Swanson NA, Tromovitch TA: Suture materials, 1980s: Properties, uses, and abuses. Int J Dermatol 21(7):373-8, Sep 1982

127. Taylor TL: Suture material: A comprehensive review of the literature. J Am Podiatry Assoc 65(7):649-61, Jul 1975

128. Tera H, Aberg C: Tensile strengths of twelve types of knot employed in surgery, using different suture materials. Acta Chir Scand 142:1-7, 1976

129. Tera H, Aberg C: The strength of suture knots after one week in vivo. Acta Chir Scand 142:301-7, 1976

130. Tera H, Aberg C: Strength of knots in surgery in relation to type of knot, type of suture material and dimension of suture thread. Acta Chir Scand 143:75-83, 1977

131. Trimbos JB, Van Rijssel EJC, Klopper PJ: Performance of sliding knots in monofilament and multifilament suture material. Obstet Gynecol 68(3):425, Sep 1986

132. Tripartite biocompatibility guidance for medical devices, 1986

133. United States Pharmacopeia, Revision XXI, 1985:

a. Physical Tests, <621> Chromatography
b. Physical Tests, <761> Nuclear Magnetic Resonance
c. Physical Tests, <851> Spectrophotometry and Light-Scattering
d. Physical Tests, <861> Sutures - Diameter
e. Physical Tests, <871> Sutures - Needle Attachment
f. Physical Tests, <881> Tensile Strength
g. Physical Tests, <661> Containers, Biological Tests -Plastics
h. Biological Tests, <85> Bacterial Endotoxins Test
i. Biological Tests, <71> Sterility

134. United States Surgical Corporation's Reclassification Petition. Docket No. 88P-0173

135. United States Surgical Corporation's letter dated May 15, 1989

136. Valcke H, Marquet JFE: Suture materials. Acta Otorhinolaryngol Belg 37(3):457-70, 1983

137. Van Winkle W Jr, Hastings JC: Considerations in the choice of suture material for various tissues. Surg Gynecol Obstet 135:113-26, July 1972

138. Van Winkle W Jr, Hastings JC, Barker E, et al: Effect of suture materials on healing skin wounds. Surg Gynecol Obstet 140:7-12, Jan 1975

139. Varma S, Ferguson HL, Breen H, et al: Comparison of seven suture materials in infected wounds - an experimental study. J Surg Res 17(3):165-70, Sep 1974

140. Varma S, Johnson LW, Ferguson HL, et al: Tissue reaction to suture materials in infected surgical wounds - a histopathologic evaluation. Am J Vet Res 42(4):563-70 Apr 1981

141. Varma S, Lumb WV, Johnson LW, et al: Further studies with polyglycolic acid (Dexon) and other sutures in infected experimental wounds. Am J Vet Res 42(4):571-4, Apr 1981

142. von Fraunhofer JA, Storey RS, Stone IK, et al.: Tensile strength of suture materials. J Biomed Mat Res 19:595-600, 1985

143. Watts DR, Carr SH, Hohf Rp: Poly(Glycolic Acid) sutures in canine vascular anastomoses. J Biomed Mater Res 10:867-77, 1976

144. Whipple AO, Elliott RE: The repair of abdominal incisions. Ann Surg 108:741, 1938

145. Wilson RS, Lelah MD, Cooper SL: Blood-material interactions. An assessment of in vitro and in vivo test methods. In Techniques of biocompatibility testing.Williams DF (ed): Boca Raton, CRC Press 2(8):151-181, 1986

146. White RA, Kopchok G, Donayre C, et al: Comparison of laser-welded and sutured arteriotomies. Arch Surg 121:1133-5, Oct 1986

147. White RA, Abergel RP, Lyons R, et al: Laser welding: An alternative method of venous repair. J Surg Res 41:260-63, 1986

148. Woodward SC, Salthouse TN: The tissue response to implants and its evaluation by light microscopy. In Handbook of biomaterials evaluation.von Recum AS (ed): New York, Macmillan Co. (30):364-378, 1986

149. Yamanaka A, Nakamae K, Takeuchi M, et al: Scanning electron microscope study on the biodegradation of IOL and suturing materials. Trans Ophthalmol Soc UK 104:517-21, 1985

150. Letters from FDA to United States Surgical Corporation granting export rights of nonabsorbable polypropylene surgical suture to The Netherlands, Italy, France, Switzerland and West Germany.

MEETING NOTICE CONFIRMATION

SUBJECT: POST 510(k) Contigency Plan for PRONOVA

DATE: FRIDAY, AUGUST 14th

TIME: 10:30 –11:30

PLACE: ERF CONFERENCE

ATTENDING: Dan Burkley, Pete Cecchini, Susan Lin, Irene Nozad, Jack Zhou & Nick Popadiuk

CALLED BY: Tom Barbolt

As stated in my previous message, attached is the reading material for this meeting.

Wanda – x3126